

evidence obtained in a cellular model of LQTS that we recently developed, we hypothesized that the augmented sodium inward current which is a consequence of the SCN5A gene defect in LQT3, would increase QT adaptation to fast rates. We tested this hypothesis in 16 genotyped LQTS patients and in 18 controls. QT interval adaptation in response to heart rate changes was derived from exercise stress test or, in children who could not perform the exercise stress test, from Holter recordings. QT was measured during stable heart rate (RR change < 10% for > 10 beats) For each 100 ms decrement of RR, QT interval shortened in controls by $2.8\% \pm 1.3\%$, in LQT1 by $4.4\% \pm 2.2\%$, in LQT2 by $3.9\% \pm 1.9\%$ and in LQT3 patients by $9.5\% \pm 3\%$ (ANOVA $p < 0.0001$; LQT3 vs LQT1, LQT2 and controls $p < 0.05$ Scheffe post hoc). These findings demonstrate differential response to heart rate changes among the three genetic variants of LQTS and suggest that LQT3 patients while presenting a marked prolongation of QT at slow rates are able to shorten QT interval at faster rates. LQT3 patients are more likely than other LQTS pts to benefit from cardiac pacing that can prevent low heart rates and the attendant excessive QT prolongation.

2:15

756-2 Diurnal and Heart Rate Dynamics of QT Interval in Symptomatic and Asymptomatic Affected Family Members of Long QT Syndrome

Heikki Swan, Matti Viitasalo, Lauri Toivonen. *Department of Medicine, Helsinki University Central Hospital, Helsinki, Finland*

Ambulatory electrocardiography was performed in 34 symptomatic (S, mean QTc 501 ms) and 35 asymptomatic but affected (As, mean QTc 485 ms) long QT syndrome (LQTS) family members, and in 22 controls. QT intervals (QT, to the end of T-wave) were measured at heart rates from 50 to 110/min in each hour where available. QT in all day-time samples representing a specified heart rate were averaged for individuals, and linear regression of QT and heart rate (HR) was determined for each group. Furthermore, QT in all samples at heart rate 60 bpm were averaged for day (10 am–8 pm) and night (10 pm–5 am) periods.

The QT/HR slope was -2.35 (ms/min $^{-1}$; $r = 0.99$) for symptomatic and -2.38 ($r = 0.98$) for asymptomatic members and -1.81 ($r = 0.99$) for controls, with respective intercepts at 640, 640 and 531 ms. No statistically significant difference existed in QT/HR slopes between S and As (multiple regression test). QT lengthened during night in each group (all $p < 0.05$). QT were similar in S and As in day time, but significantly longer in S than in As during night (table):

	S	As	Control	p (S vs. As)
QT day	501 ± 36	485 ± 30	421 ± 16	NS
QT night	531 ± 42	498 ± 31	441 ± 16	0.003

QT interval behavior in multiple heart-rate based samples in ambulatory ECG may be unable to separate symptomatic from asymptomatic but affected LQTS relatives. In contrast, the symptomatic members are characterized by a greater circadian variation with more marked QT interval lengthening at night.

2:30

756-3 Dynamic Relation Between Ventricular Repolarization and Heart Rate in the Long QT Syndrome

Emanuela H. Locati, Marco Stramba-Badiale, Silvia G. Priori, Carlo Napolitano, Alessandra Martinelli, Peter J. Schwartz. *Dept of Med, Univ of Milan, IT; Dept of Cardiol, Univ of Pavia, IT*

In long QT syndrome (LQTS) the dynamic relation between the early portion of QT interval (QTp) and heart rate was previously reported to be impaired. However, QTP may not correspond to the entire QT interval (QTc), also including the terminal portion more likely to be affected in LQTS. We analyzed the relation between QTP and QTc and cycle length (RR) in the 24-hour Holter recordings of 32 LQTS patients (56% females, mean age 21 ± 15 years, 75% with history of syncope/cardiac arrest, 56% on beta-blockers, BB) and of 32 normal subjects (C) with similar gender and age distribution. A new algorithm (ELA Medical) automatically measured QTP and QTc from 2880 30-sec templates and computed the rate corrected QTc and QTP (QTec, QTpc, ms) and linear regression slopes (QTP/RR and QTc/RR):

	RR	QTec	QTpc	QTc/RR	QTP/RR
Controls (n = 32)	809 ± 126	408 ± 20	313 ± 19	0.15 ± 0.04	0.18 ± 0.04
Pts w/out BB (n = 14)	801 ± 114	439 ± 30	405 ± 32	0.31 ± 0.15	0.28 ± 0.12
Pts with BB (n = 18)	949 ± 125	493 ± 32	392 ± 32	0.24 ± 0.10	0.21 ± 0.09

QTc/RR and QTP/RR were steeper in LQTS pts than in C ($p < 0.0001$).

LQTS pts without BB tended to have steeper slopes than pts on BB ($p = 0.06$). QTP/RR was steeper than QTc/RR ($p < 0.0001$) in C, while in LQTS pts with BB the reverse was true ($p < 0.01$). Thus both QTP/RR and QTc/RR may help to characterize the altered adaptation of QT interval to heart rate in LQTS. Slopes were more disperse in LQTS pts than in C ($p < 0.0001$), suggesting possible heterogeneity of the dynamic relation of QT interval and heart rate in patients with different risk factors and genetic background.

2:45

756-4 Age and Gender-Related Differences in the Congenital Long QT Syndrome: Findings From the International Prospective Study

Emanuela H. Locati, Arthur J. Moss, Peter J. Schwartz, G. Michael Vincent, Michael H. Lehmann, Jennifer L. Robinson, Katherine Timothy, Wojciech Zareba, Silvia G. Priori, Mark Andrews, Moonseong Heo, W. Jackson Hall. *Dept of Cardiol, Univ of Pavia, Italy; Dept of Comm and Prev Medicine, Univ of Rochester, NY*

In the long QT syndrome (LQTS) international prospective study an unexplained gender imbalance was consistently observed. Females (F) were prevalent (70%, $p < 0.0001$) among 428 index cases (Proband, P). Among their 4118 family members (FM), F were prevalent in the 256 FM with history of syncope/cardiac arrest (60%, $p = 0.03$) and in the 200 FM with unexplained sudden death before age 50 yrs (59%, $p = 0.06$). However, among P the age-adjusted probability of events (syncope/cardiac arrest/unexplained sudden death) by Kaplan-Meier survival analysis using birth as time of origin was 71% in M and 44% in F by age 15 yrs ($p = 0.025$), while it was similar in M and F by age 50 yrs (95% vs 90%, ns). By Cox proportional models, the risk of events was higher in M (hazard ratio 1.45; C.I. 1.12–1.85; $p < 0.005$), and particularly in M before age 15 yrs (1.91; 1.43–2.54; $p < 0.0001$), while F were at risk of events after age 15 yrs (1.67; 0.92–3.03; $p = 0.055$). QTc duration (1.02 per 10 ms increments; 1.01–1.04; $p = 0.025$) and deafness (1.74; 1.10–2.75; $p = 0.025$) were independent risk factors in both genders. Similarly, in FM risk factors were first degree relation to P (2.04; 1.55–2.67; $p < 0.001$), deafness (3.17; 1.01–9.91; $p = 0.04$), QTc duration (1.13; 1.01–1.15; $p < 0.0001$) and F gender after age 15 yrs (2.41; 1.47–3.95; $p < 0.005$). These findings suggest that in long QT syndrome males have a higher risk of events until puberty, while females remain at risk of events later in life.

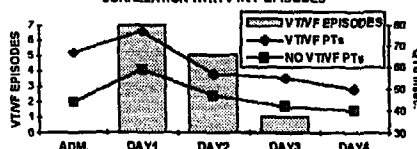
3:00

756-5 QT Dispersion During Acute Myocardial Infarction: Correlation With Malignant Ventricular Arrhythmias

Gaetano Barbato, Rosaria di Niro, Nicoletta Franco, Maurizio Mezzetti, Pier Camillo Pavesi, Daniele Bracchetti. *Dep. Cardiology, Maggiore Hospital, Bologna, Italy*

The aim of the study was to evaluate the correlation between the degree of QT dispersion (QTd) and ventricular tachycardia (VT) or fibrillation (VF) in patients (Pts) with acute myocardial infarction (AMI) and particularly to verify the potential correlation between QTd and the onset of VT/VF. For this purpose we evaluated 97 Pts, 78 male and 19 female, with mean age 63 ± 10 , admitted consecutively to the CCU because of AMI. 44/97 Pts (45.3%) were treated with fibrinolytic therapy. In every PT we estimated through a computerized system (HP M1700A) the duration of the QT interval in each of the 12 standard leads of the surface ECG. The value of QTd was estimated by subtracting the lowest value of QT from the highest. In order to avoid miscalculation due to artefacts or low amplitude T waves, we estimated the value of QTd by analyzing ten leads excluding the highest and lowest value of 12 leads and those values with a T wave less than 0.15 mV. QTd was calculated daily for the first 4 days. We excluded from the study Pts with arrhythmias, or large QRS complex at the ECG or contemporary therapy with drugs that can change the QT and Pts over 80 years in age. **Results:** 13/97 Pts (13%) had VT/VF during AMI (group 1) and 84 Pts (86%) did not have VT/VF (group 2). The average value of QTd in groups 1 and 2 respectively was: admission 67 ms vs. 43 ms ($p < 0.0001$), 1st day 76 ms vs. 59 ms ($p < 0.01$), 2nd day 56 ms vs. 49 ms ($p = ns$), 3rd day 59 ms vs. 44 ms ($p < 0.5$), 4th day 52 ms vs. 42 ms ($p < 0.5$). No significant difference in QTc duration was observed between the two groups of Pts. The correlation between the occurrences of the arrhythmia episodes and QTd is shown in the figure.

QT DISPERSION DURING MYOCARDIAL INFARCTION: CORRELATION WITH VT/VF EPISODES



Discussion: high values of QTd appear to be linked to high rate of occurrence of VT/VF during AMI considering that PTs of group 1 had significantly higher value of QTd than PTs of group 2. We observed 92% of the total VT/VF episodes during days 1 and 2, the days in which QTd was greatest. **Conclusion:** Elevated values of QTd are correlated with high incidence of VT/VF during AMI.

3:15

756-6 Mortality in the Survival With Oral D-sotalol (SWORD) Trial: Why Did Patients Die?

Craig M. Pratt, A. John Camm, William Cooper, Peter L. Friedman, Daniel J. MacNeil, Kathleen M. Moulton, Bertram Pitt, Peter J. Schwartz, Enrico P. Veltri, Albert L. Waldo for the SWORD Investigators. Baylor College of Medicine, Houston, Texas, USA

The SWORD trial assessed the effect of oral d-sotalol on patients (pts) surviving myocardial infarction (MI) with an ejection fraction (EF) $\leq 40\%$ and included two index MI groups: recent (6–42 days), and remote (> 42 days) with clinical heart failure (CHF); N = 915 and 2206, respectively. The trial was discontinued when the statistical boundary for harm was crossed [relative risk (RR) = 1.65; $p = 0.006$]; with approximately 2/3 of the deaths presumed arrhythmic. We investigated the nature of d-sotalol associated risk. Each index MI group (recent and remote) was divided into EF $\leq 30\%$ vs. 31–40%. The d-sotalol associated mortality was not uniformly distributed in these four groups, being greatest in the remote MI, EF 31–40% group (N = 1180) and was lowest in the remote MI, EF $\leq 30\%$ group (N = 1026); [RR = 7.9 and 1.0; $p = 0.02$]. While traditional MI risk factors were significantly related to increased mortality in the entire SWORD population (age, EF, CHF class, diuretics, digoxin) only aspirin and beta blockers were associated with a lower mortality risk. Variables known to be associated with Torsades de pointes (TdP) [time from treatment, dose, QTc, bradycardia, electrolytes, diuretics] were not differentially predictive of d-sotalol associated risk; whereas female gender was (RR = 4.7; 95% C.I. = 1.4–16.5). Deaths in females were not uniformly distributed, occurring mostly in the recent MI group ($p = 0.005$). Both ventricular premature complexes and nonsustained ventricular tachycardia (VT) increased risk in the entire SWORD population, but VT increased d-sotalol associated risk differentially, mostly in the remote MI group ($p = 0.02$). Nonfatal serious arrhythmic events (cardiac arrest, ventricular fibrillation, sustained VT) were rare in both placebo and d-sotalol assigned pts; there were only two nonfatal TdP events in d-sotalol vs. none in placebo assigned pts. **Conclusions:** 1) presumed arrhythmic death accounted for the majority of deaths in both placebo (67%) and d-sotalol (72%) assigned pts; 2) the majority of d-sotalol associated risk was in pts remote from MI with EF 31–40%; 3) except for female gender, no other known risk factors supported TdP as the mechanism for the d-sotalol associated mortality risk.

757 Echo Doppler Assessment of Diastolic Function

Tuesday, March 26, 1996, 2:00 p.m.–3:30 p.m.
Orange County Convention Center, Room 315

757-1 Is Doppler Echo a Non-Invasive Alternative to Swan-Ganz Catheterization in Patients With Advanced Heart Failure?

James H. Stein, Alex Neumann, Lynn M. Preston, Jeffrey S. Soble, Susan M. Quinn, Joseph E. Parrillo, Maryl R. Johnson, Richard H. Marcus. Rush Medical College, Chicago, Illinois

Each of the hemodynamic parameters obtained by Swan-Ganz catheterization is theoretically accessible using Doppler echo methods. Although acceptable correlation between invasive (INV) and non-invasive (NI) measurements has been demonstrated in patient populations, acceptable agreement in individual patients must be demonstrated before these techniques can be implemented clinically. **Methods:** INV measurements of right atrial (RA), PA systolic (PAS), PA diastolic (PAD), PA mean (PAM), and pulmonary capillary wedge (PCW) pressures (mmHg) and thermodilution cardiac output (CO, L/min) were compared with NI estimates in 15 heart failure patients. NI data included: RA by IVC size and respirophasic change, PAS = $4[\text{peak TR velocity}]^2 + \text{RA}$, PAD = $4[\text{pulmonary insufficiency end-diastolic velocity}]^2 + \text{RA}$, PAM = PAD + $1/3$ [PAS – PAD], PCW = diastolic BP – $4[\text{MR velocity at aortic valve opening}]^2$, CO = $[\text{transaortic velocity-time integral}] [\text{aortic annular area}] [\text{HR}]$.

Results: All hemodynamic parameters could be determined noninvasively in 80% of patients. INV and NI parameters correlated well ($r > 0.95$, $p <$

	RA	PAS	PAD	PAM	PCW	CO
Range (INV)	5–29	20–80	9–42	13–51	7–42	3.10–7.62
Mean Δ (INV – NI)	0	–108	0.67	0.38	3.67	0.08
$\pm 95\%$ confidence	4.44	4.26	5.04	2.66	3.50	0.58

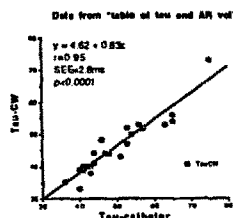
0.001 for all). Bias (mean Δ) was small and the limits of agreement between the INV and NI measurements were narrow. **Conclusion:** NI estimates of invasively measured hemodynamic parameters are sufficiently accurate for clinical application in individual patients with advanced heart failure.

2:15

757-2 Assessment of Left Ventricular Relaxation by Continuous-Wave Doppler Echocardiography: Accuracy of Measurement of the Time Constant Tau: An Animal Study

Xiaodong Zhou, Michael Jones, Takahiro Shiota, Dag Teien, Shuping Ge, Masahiro Ishii, David J. Sahn. Oregon Health Sci Univ, Portland, OR; NIH-LAMS, Bethesda, MD

The time constant of isovolumic relaxation ($-\text{dp}/\text{dt}_{\text{max}}$) [Tau (τ)] is an important index of left ventricular (LV) diastolic function, but the need for invasive measurement with high-fidelity catheters has limited its use in clinical cardiology. The purpose of this study to compare the relationship between τ -derived from aortic regurgitant velocity spectra (τ -AR) and catheter-derived values and to evaluate the effects of different hemodynamics and regurgitation volumes on the τ -AR. **Methods:** In 6 sheep, chronic AR was surgically created and 24 hemodynamically different states were achieved pharmacologically. Peak AR flow rate, regurgitant stroke volume and regurgitant fraction were derived using pulmonary and aortic electromagnetic flow meters. The CW Doppler aortic regurgitant velocity spectrum was recorded simultaneously with high-fidelity LV and aortic pressure. The time interval from the onset of AR to the point at $(1 - 1/e)^{1/2}$ of the maximal AR velocity was determined as an estimate of the time constant τ .



The Doppler estimate showed a good correlation to catheter-derived τ ($r = 0.95$, SEE = 2.8 ms $p < 0.0001$, Fig.) and was not significantly affected by regurgitant flow rate or forward cardiac output.

757-3 A Novel Approach of Analyzing Color M-Mode Doppler Filling Patterns by Automated Computer Eigenvectors

Marie Stugaard, Neil Greenberg, Pieter M. Vandervoort, James D. Thomas. Cardiovascular Imaging Center, Cleveland Clinic Foundation, Cleveland, OH

Color M-mode Doppler echocardiography is a promising approach to the study of left ventricular (LV) diastolic function. However, the previous methods for analyzing these images have limitations, and factors related to machine settings have not been studied. To address these issues, a new and automated method by the use of computer algorithms was applied. **Methods:** Ten healthy volunteers with normal ventricles and 5 patients with left ventricular dysfunction (coronary artery disease or cardiomyopathy) were included. The area of interest, the E-wave, was defined, using an automatic algorithm to connect the unaltered and aliased components of the filling wave. These velocities were divided into 3 bands using a percentage of the maximum velocity (0–50%, 25–75%, 50–100%). For each velocity band, an eigenvector analysis was performed to compute the principal components of the E-wave (see figure). The resulting centroid (s.t.), angle of rotation (ϕ), and eigenvalues (λ_1 , λ_2) describe the spatiotemporal velocity distribution. The eigenvalues represent the width in each of the principle directions.

Results: The different instrument settings, which included packet size, wall filter and spatial filter, did not influence any of the above parameters ($p = \text{NS}$ by analysis of variance). The overall results showed that s and Θ ; were most significant in separating the two study populations. In the 25–75% band, s was -0.88 ± 0.17 cm in normals vs. -1.79 ± 0.29 cm ($p < 0.05$) in